

R<sub>1</sub>  
cont. the insert sequences of the insert library comprise a second nucleotide sequence encoding a second polypeptide subunit which varies within the insert library, each of the insert sequences comprising a 5'- and 3'- flanking sequence at the respective ends of the insert sequence and being sufficiently homologous to the 5'- and 3'-terminus sequences of the linearized yeast expression vector, respectively, to enable homologous recombination to occur, and

the first and second polypeptide subunits are capable of being expressed as separate proteins and assembling to form the library of protein complexes of the first and second polypeptide subunits and having a diversity of at least  $1 \times 10^6$ .

Please add the following new claims:

97. (New) The method of claim 54, wherein the first polypeptide subunit comprises an antibody heavy-chain region, and the second polypeptide subunit comprises an antibody light-chain region.

98. (New) The method of claim 97, wherein the first polypeptide subunit further comprises an antibody heavy chain constant 1 region, and the second polypeptide subunit further comprises an antibody light chain constant region.

99. (New) The method of claim 97, wherein the source of the coding sequences of the antibody light-chain and heavy-chain regions is from human, non-human primate, or rodent DNA.

100. (New) The method of claim 97, wherein the source of the coding sequences of the antibody light-chain and heavy-chain variable regions is from one or more non-immunized animals.

101. (New) The method of claim 97, wherein the source of the coding sequences of the antibody light-chain and heavy-chain variable regions are selected from the group consisting of human fetal spleen, fetal liver, bone marrow, lymph nodes and peripheral blood cells.

102. (New) The method of claim 54, wherein the diversity of the first and the second polypeptide subunits each independently is at least  $1 \times 10^3$ .

103. (New) The method of claim 54, wherein the diversity of the first and the second polypeptide subunits each independently is at least  $1 \times 10^4$ .

~~104~~ (New) The method of claim ~~54~~, wherein the diversity of the first and the second polypeptide subunits each independently is at least  $1 \times 10^5$ .

~~105~~ (New) The method of claim ~~54~~, wherein the diversity of the protein complexes is at least  $1 \times 10^7$ .

~~106~~ (New) The method of claim ~~54~~, wherein the diversity of the protein complexes is at least  $1 \times 10^{10}$ .

~~107~~ (New) The method of claim ~~54~~, wherein the first polypeptide subunit further comprises an activation domain or a DNA binding domain of a transcription activator.

~~108~~ (New) The method of claim ~~107~~, wherein the transcription activator is selected from the group consisting of GAL4, GCN4, and ADR1 transcription activator.

#### REMARKS

The present Amendment is in response to the Examiner's Office Action mailed June 17, 2002. Claim 54 is amended. New claims 97-108 are added. Claims 54-61 and 97-108 are pending.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

#### I. Obviousness Rejection under 35 U.S.C. §103 over Motwani et al. and Fusco et al.

The Examiner rejects claims 54-61 under 35 U.S.C. § 103(a) as being unpatentable over Motwani et al. (US Patent No: 6,358,733) and Fusco et al. (1999) Yeast 15:715-720.

Independent claim 54 as amended specifies a method for constructing a library of yeast expression vectors encoding a **library of protein complexes**. Each of the protein complexes is formed by the first ( $V_1$ ) and second ( $V_2$ ) polypeptide subunits, such as antibody  $V_H$  and  $V_L$ . The diversity of the first polypeptide subunit is at least  $1 \times 10^3$  and the diversity of the protein